



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/774,278 | 01/30/2001 | Gregory M. Lanza | 4375-000004/US | 2535 |
| 25225 | 7590 | 10/20/2004 | | |
| MORRISON & FOERSTER LLP 3811 VALLEY CENTRE DRIVE SUITE 500 SAN DIEGO, CA 92130-2332 | | | | |
| EXAMINER | | | | |
| SHARAREH, SHAHNAM J | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1617 | | | | |

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/774,278

Applicant(s)

LANZA ET AL.

Examiner

Shahnam Sharareh

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,7,8,13,17,18,21,25,26,31,35 and 68-77 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 7-8, 13, 17-18, 21, 25-26, 31, 35, 68-77 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f):
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Amendment filed on August 5, 2004 has been entered. Any rejection that is not addressed in this Office Action is considered obviated in view of the amendments made to the pending claims. Claims 1, 3, 7-8, 13, 17-18, 21, 25-26, 31, 35, 68-77 are pending.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 7-8, 13, 17-18, 25-26, 31, 35, 68-72, 74, 76-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by Ostenson US Patent 6,375,931.

Applicant's arguments with respect to this rejection have been fully considered but are not found to be persuasive.

As the initial matter, Examiner takes the position that the scope of the instant claims are directed to methods of comparing acoustic reflectivity of a target for ultrasound imaging comprising measuring reflectivity prior to raising the temperature of the liquid nanoparticles bound to a target, raising the temperature of said nanoparticles, measuring reflectivity after said rise of temperature and determining the change in reflectivity of the nanoparticles before and after the raising of the temperature.

Thus, Examiner interprets the pending claims to be directed to methods of performing ultrasound imaging comprising having liquid bound nanoparticles on a target area, measuring reflectivity of said liquid bound nanoparticles, raising the temperature of the liquid bound nanoparticles, measuring the reflectivity of the liquid bound nanoparticles after said raising of the temperature, and determining the change in

Art Unit: 1617

reflectivity. Having such interpretation in mind, Ostenson anticipates all limitation of the instant claims.

Note that such recitations, as “comparing acoustic reflectivity at a lower and a higher temperature” are viewed to be inherent in any methods of ultrasound imaging that performs the instantly claimed method steps, because a continuous exposure to the ultrasound energy during an ultrasound imaging procedure inherently raises local temperature. (see Ostenson at col 5, lines 5-46). Thus, the ultrasound imaging begins at a lower temperature (local temperature at the beginning of the imaging procedure) and ends at a higher temperature (local temperature at the end of the imaging procedure) on a specific site. Since Ostenson describes the instantly claimed method steps, Ostenson also anticipates the instant limitation of “comparing acoustic reflectivity at a lower and higher temperature.”

Applicant argues that Ostenson is dealing with gas dispersion. (Arguments at page 6). Yet, the instant claims are directed to measuring the reflectivity of nanoparticles where the nanoparticles are in liquid form. Id.

In reply Examiner first states that Ostensen clearly teaches exposure of his nanoparticles when in the form of an emulsion. (col 44, lines 5-67). Therefore, before ultrasound energy is applied, the nanoparticles of Ostenson at the site comprise a liquid perfluorocarbon. It is only after the exposure of the ultrasound energy that Ostenson's formulation starts to generate gas and thereby expand gaseous microbubbles in vivo. (see entire col 36-37 and all examples of col 44). Therefore, Ostenson meets the

limitation of instant step (a), because he teaches the use of liquid droplets at a site of interest prior to application of ultrasound.

Secondly, the scope of the instant claims never exclude formation of gaseous moieties after the raising the temperatures locally. The instant step (b)–(d) does not exclude formation of a gas within the nanoparticles. Therefore, Ostenson's step of applying continuous ultrasound energy meets the limitations of instant steps (b)–(d). The fact that Ostenson's contrast medium gas expands is not a teaching away from the instant claims, because such process is not excluded in the instant claims.

Third, Ostensen discloses methods of performing ultrasound imaging comprising administering a perfluorocarbon emulsion comprising such perfluorocarbons as perfluoropentane, perfluorohexane, and even perfluorooctane to a specific region of a patient (see abstract, col 8, lines 1-60). Such perfluorocarbons are the same as those instantly envisioned.

Ostenson teaches droplets that are smaller than 10 μm and thus meets the limitations of the instant nanoparticles, because the sizes of the instant nanoparticles as described in page 21, line 7-10 of the specification encompass particles as large as 10 μm . (see 9, lines 34-38; col 35-37, and claim 4 wherein various perfluorocarbon emulsion mixtures are described). Thus, Ostenson meets the carrier system of the instant claims.

Ostenson clearly describes preparation of perfluorodecalin:perfluorobutane emulsions which is not a gaseous dispersion. (col 22, lines 14-55). In fact, Ostenson specifically explains that his gaseous compositions are not entirely consisting of gas;

Art Unit: 1617

rather, they may be partially of gas, liquid, or gaseous precursors (col 3, lines 9-20).

Certainly perfluoropentane, and perfluorohexanes are not a gas at room temperature or before they are applied in vivo (col 3, lines 50-65). They may convert to a vapor or gas when subject to ultrasound energy or a rise of local temperature at the site of interest.

The instant claims do not exclude the formulations of Ostenson, nor do the claims exclude formation of gas after the instant liquid nanoparticles are exposed to ultrasound energy or a rise in the local temperature. Therefore, the instant process steps falls within those described by Ostenson.

Applicant also states that it is not clear why Examiner asserts that perfluorobutane is a liquid at room temperature when the Ostensen itself states that at 9 deg C, the perfluorobutane is in the form of microbubbles. See Arguments at page 6, 3rd para. In response, Examiner states that 9 deg C is not the room temperature. Therefore, such statement by the patent is not contrary to Examiner's position.

Further, Ostenson's microbubbles are not free of liquid, in fact they may be partially liquid or fully of gaseous precursors. (col 3, lines 9-65). Example 5 and 10 of Ostenson describes Ostensen's process steps wherein a perfluorocarbon emulsion is administered to a mammal. Ostenson then teaches imaging of a specific site such as heart or kidney. Ostenson specifically expresses a steady rise in enhancement of the contrast images (see col 39-40). As described by Ostensen, this steady rise of resonance intensity is attributed to an increase in microbubble size which is respectively caused by an increase in temperature of at least 5 Deg C of the perfluorocarbon liquid within the microbubbles of Ostensen.

Art Unit: 1617

Ostenson does not state that at the end of his procedure all perfluorobutane or perfluorodecaline:perfluorobutane emulsion is converted to gas. Neither does he say that that after a rise of atleast a 5 deg C increments the entire microbubble is filled with gas. Rather, the teaching is implicit as to the conversion of at least a portion of perfluorocarbon gaseous precursors or emulsion to gas. It goes without saying that Ostenson shows a steady rise of the size of the microbubbles. Thus, at any degree rise of temperature more gaseous precursors are converted to gas to intensify the expansion of the microbubbles in vivo. Applicant has not yet provided any evidence to show the contrary.

Further, Applicant appears to misinterpret the teachings of Ostensen. Ostensen states in col 35, line 10:

Analysis of the perfluorobutane gas dispersion alone showed that at 9° C. 52% of the microbubbles were of size below 9.9 µm; this proportion was reduced to 31% when the temperature had increased to 37° C. This temperature change was accompanied by a corresponding increase in the proportion of microbubbles in the size range 15-50 µm, from 8% to 42%.

again, such statement is not viewed to mean that perfluorobutane is not a gas at room temperature, because 9 deg C is not room temperature. Thus, as reasoned in the previous Office Action and given the fact that perfluorobutane, perfluoropentane, perfluorohexane, and perfluoroheptanes are liquid at room temperature, and that microparticles containing such compounds increase in size when subject to ultrasound frequency as described above, the Examiner maintains the position that the continuous ultrasound imaging over a period of time of a specific site, as described by Ostenson, is essentially a measurement of the change in reflectivity of contrast microbubbles wherein

Art Unit: 1617

the size of these microbubbles are increased subsequent to a rise of temperature, because the intensity of contrast increases with the duration of exposure to the ultrasound frequency. Applicant has not provided any evidence to show otherwise.

Therefore, Examiner maintains position that the such sequence of steps described in Ostenson's patent meet the steps (a)-(d) of the instant claim 1.

Claim Rejections - 35 USC § 103

Claims 1, 3, 7-8, 13, 17-18, 21, 25-26, 31, 35, 68-77 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ostenson.

Applicant's arguments with respect to this rejection have been fully considered but are not perssuive. Applicant argues that Ostenson is solely directed to gaseous dispersions. However, for the reasons argued above Examiner believes that Ostenson envisioned the use of liquid or gaseous precursors. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify Ostenson's method and employ other art equivalent perfluorocarbon liquids such as perfluorooctane in humans

Conclusion

No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

Art Unit: 1617

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SS


RUSSELL TRAVERS
PRIMARY EXAMINER